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**Subject:** STICS: Clearance Completion: #ORD-017647: A conceptual framework to advance exposure science research and complement the Adverse Outcome Pathway framework

The clearance for this CSS product is complete:

- **Product type, subtype:** Presentations and Technical Summaries, Poster
- **Product title:** A conceptual framework to advance exposure science research and complement the Adverse Outcome Pathway framework
- **Author(s):** Edwards, S,C. Tan,J. Leonard,P. Egeghy and J. Teeguarden
- **Initiator:** Stephen Edwards,ord/nheerl/istd
- **ORD Tracking Number:** Tracking # ORD-017647
- **Product Description / Abstract:** A tremendous amount of data on environmental stressors has been accumulated in exposure science, epidemiology, and toxicology, yet most of these data reside in different silos. The Adverse Outcome Pathway (AOP) framework was developed as an organizing principle for toxicological information, and an international repository has been built for this information (<http://aopkb.org/>). This has enabled better collaboration and information exchange within the research community; it also provides a more uniform representation of mechanistic information for the risk assessment and regulatory communities. The Aggregate Exposure Pathway (AEP) is essentially an integrated exposure framework, which serves as a complement to the AOP. The AEP is completely consistent with the construct of conceptual site models (CSM) developed in cumulative risk assessment (CRA) and can serve to bring technological advances such as the AOP into such applications. Ideally, the AEP also includes absorption, distribution, metabolism, and excretion within a biological receptor in order to reach a target site exposure (i.e., dose) at the cellular/tissue level. This would better match exposure predictions with the molecular initiating events described in the AOP framework and allow better integration of high throughput, in vitro toxicity data. The AEP framework is based on two fundamental components inspired by AOPs. A Key Exposure State (KES) represents a measurable stock of a stressor within the environment or the receptor. A Key Transformation/Transportation Relationship (KTR) represents the movement of the stressor or conversion of a stressor into a different one. The AEP framework will be illustrated through a set of case studies including phthalates and other environmental stressors. The AEP builds on previous constructs in exposure and risk assessment science such as exposure pathways, conceptual site models, and stocks/flows from systems modeling. A harmonized framework allows information from one construct to flow into another, which should enhance interoperability among computational models. As with the AOP framework, a unified representation of the information should also help in translating research results to inform regulatory decisions.
- **Tracking and Planning**
  - Task ID: CSS17.01.01
  - Task: RMS AOP Discovery and Development task
  - Product Title: N/A - Not Applicable
  - Product Description: N/A - Not Applicable
  - Project: AOP Discovery and Development

- Topic: Complex Systems Science
- Research Program Area: CSS
  
- **Product Category:** Does not require Advance Notification
- **QA form attached in STICS?:** Yes
- **QAPP Reference:** IRP-NHEERL/ISTD/IO/SWE/2014-01-r1
- **Keywords:**
  - adverse outcome pathway (AOP)
  - aggregate exposure pathway (AEP)
  - AOP knowledgebase (AOPKB)
  - ADME
  
- **Meeting Information:**
  - Meeting Name: Society of Toxicology
  - Meeting Start Date: 03/12/2017
  - Meeting End Date: 03/16/2017

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